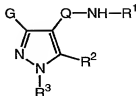


Claims

1. A compound of formula I:



I

or a pharmaceutically acceptable derivative thereof,
wherein:

R^1 is selected from hydrogen, CONH_2 , $\text{T}_{(n)}\text{-R}$, or $\text{T}_{(n)}\text{-Ar}^1$;

R is an aliphatic or substituted aliphatic group;

n is zero or one;

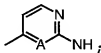
T is C(=O) , CO_2 , CONH , S(O)_2 , $\text{S(O)}_2\text{NH}$, COCH_2 or CH_2 ;

R^2 is selected from hydrogen, -R, $-\text{CH}_2\text{OR}$, $-\text{CH}_2\text{OH}$, $-\text{CH=O}$,
 $-\text{CH}_2\text{SR}$, $-\text{CH}_2\text{S(O)}_2\text{R}$, $-\text{CH}_2\text{(C=O)R}$, $-\text{CH}_2\text{CO}_2\text{R}$, $-\text{CH}_2\text{CO}_2\text{H}$, -
 CH_2CN , $-\text{CH}_2\text{NHR}$, $-\text{CH}_2\text{N(R)}_2$, $-\text{CH=N-OR}$, $-\text{CH=NNHR}$, -
 CH=NN(R)_2 , $-\text{CH=NNHCOR}$, $-\text{CH=NNHCO}_2\text{R}$, $-\text{CH=NNHSO}_2\text{R}$, -
 aryl, $-\text{CH}_2(\text{aryl})$, $-\text{CH}_2\text{NH}_2$, $-\text{CH}_2\text{NHCOR}$, $-\text{CH}_2\text{NHCONHR}$, -
 $\text{CH}_2\text{NHCON(R)}_2$, $-\text{CH}_2\text{NRCOR}$, $-\text{CH}_2\text{NHCO}_2\text{R}$, $-\text{CH}_2\text{CONHR}$, -
 $\text{CH}_2\text{CON(R)}_2$, $-\text{CH}_2\text{SO}_2\text{NH}_2$, $-\text{CH}_2(\text{heterocyclyl})$, or -
 (heterocyclyl);

R^3 is selected from hydrogen, -R, hydroxyalkyl,
 alkoxyalkyl, alkylthioalkyl, aminoalkyl,
 alkylaminoalkyl, dialkylaminoalkyl, heterocyclyl,
 heterocyclylalkyl, aryl, aralkyl, or aryloxyalkyl;

G is hydrogen or C_{1-3} alkyl;

Q-NH is



wherein the H of Q-NH is optionally replaced by R, COR,
S(O)₂R, or CO₂R;

A is N or CH;

Ar¹ is aryl, substituted aryl, heterocyclyl or
substituted heterocyclyl, wherein Ar¹ is optionally
fused to a partially unsaturated or fully unsaturated
five to seven membered ring containing zero to three
heteroatoms;

wherein each substitutable carbon atom in Ar¹, including
the fused ring when present, is optionally and
independently substituted by halo, R, OR, SR, OH,
NO₂, CN, NH₂, NHR, N(R)₂, NHCOR, NHCONHR, NHCON(R)₂,
NRCOR, NHCO₂R, CO₂R, CO₂H, COR, CONHR, CON(R)₂,
S(O)₂R, SONH₂, S(O)R, SO₂NHR, or NHS(O)₂R, and wherein
each saturated carbon in the fused ring is further
optionally and independently substituted by =O, =S,
=NNHR, =NNR₂, =N-OR, =NNHCOR, =NNHCO₂R, =NNHSO₂R, or
=NR; and

wherein each substitutable nitrogen atom in Ar¹ is
optionally substituted by R, COR, S(O)₂R, or CO₂R.

2. The compound of claim 1 having at least one
feature selected from the group consisting of:

(a) R¹ is selected from hydrogen, T_(n)-R, or T_(n)-
Ar¹;

(b) R² is selected from hydrogen, -R, -CH₂OR,
CH₂OH, CH₂(heterocyclyl), -CH₂(substituted
heterocyclyl), -(heterocyclyl), or -(substituted
heterocyclyl);

(c) R³ is selected from -R, heterocyclyl,
heterocyclylalkyl, aryl, or aralkyl and;

(d) G is hydrogen or methyl.

3. The compound of claim 2 wherein:

- (a) R^1 is selected from hydrogen, $T_{(n)}-R$, or $T_{(n)}-Ar^1$;
- (b) R^2 is selected from hydrogen, $-R$, $-CH_2OR$, CH_2OH , CH_2 (heterocyclyl), $-CH_2$ (substituted heterocyclyl), $-(heterocyclyl)$, or $-(substituted heterocyclyl)$;
- (c) R^3 is selected from $-R$, heterocyclyl, heterocyclylalkyl, aryl, or aralkyl and;
- (d) G is hydrogen or methyl.

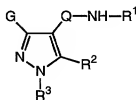
4. The compound of claim 3 wherein G is hydrogen or methyl; R^1 is selected from phenyl, cyclohexyl, pyridyl, naphthyl, or quinolinyl; R^2 is selected from hydrogen, methyl, alkoxymethyl, benzyloxymethyl, or heterocyclylmethyl; and R^3 is phenyl or benzyl; wherein each of R^1-R^3 is optionally substituted.

5. The compound of claim 3 wherein G is hydrogen or methyl; R^1 is phenyl or cyclohexyl; R^2 is methoxymethyl, methoxyethoxymethyl, ethoxymethyl, piperidin-1-ylmethyl, morpholin-4-ylmethyl, or tetrahydrofuran-3-ylmethyl; and R^3 is phenyl or benzyl; wherein each of R^1-R^3 is optionally substituted.

6. A compound selected from the compounds listed in Table 1.

7. A method for treating a disease or condition in a mammal that is alleviated by treatment with a JNK kinase inhibitor, comprising administering to a mammal

in need of such a treatment a therapeutically effective amount of a compound of formula I:



I

or a pharmaceutically acceptable derivative thereof, wherein:

R^1 is selected from hydrogen, CONH_2 , $\text{T}_{(n)}\text{-R}$, or $\text{T}_{(n)}\text{-Ar}^1$;

R is an aliphatic or substituted aliphatic group;

n is zero or one;

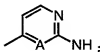
T is C(=O) , CO_2 , CONH , S(O)_2 , $\text{S(O)}_2\text{NH}$, COCH_2 or CH_2 ;

R^2 is selected from hydrogen, -R, $-\text{CH}_2\text{OR}$, $-\text{CH}_2\text{OH}$, $-\text{CH=O}$, $-\text{CH}_2\text{SR}$, $-\text{CH}_2\text{S(O)}_2\text{R}$, $-\text{CH}_2\text{(C=O)R}$, $-\text{CH}_2\text{CO}_2\text{R}$, $-\text{CH}_2\text{CO}_2\text{H}$, $-\text{CH}_2\text{CN}$, $-\text{CH}_2\text{NHR}$, $-\text{CH}_2\text{N(R)}_2$, $-\text{CH=N-OR}$, $-\text{CH=NNHR}$, $-\text{CH=NN(R)}_2$, $-\text{CH=NNHCOR}$, $-\text{CH=NNHCO}_2\text{R}$, $-\text{CH=NNHSO}_2\text{R}$, $-\text{aryl}$, $-\text{CH}_2\text{(aryl)}$, $-\text{CH}_2\text{NH}_2$, $-\text{CH}_2\text{NHCOR}$, $-\text{CH}_2\text{NHCONHR}$, $-\text{CH}_2\text{NHCON(R)}_2$, $-\text{CH}_2\text{NRCOR}$, $-\text{CH}_2\text{NHCO}_2\text{R}$, $-\text{CH}_2\text{CONHR}$, $-\text{CH}_2\text{CON(R)}_2$, $-\text{CH}_2\text{SO}_2\text{NH}_2$, $-\text{CH}_2\text{(heterocyclyl)}$, or $-\text{(heterocyclyl)}$;

R^3 is selected from hydrogen, -R, hydroxyalkyl, alkoxyalkyl, alkylthioalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, or aryloxyalkyl;

G is hydrogen or C_{1-3} alkyl;

Q-NH is



wherein the H of Q-NH is optionally replaced by R, COR, $\text{S(O)}_2\text{R}$, or CO_2R ;

A is N or CH;

Ar¹ is aryl, substituted aryl, heterocyclyl or substituted heterocyclyl, wherein Ar¹ is optionally fused to a partially unsaturated or fully unsaturated five to seven membered ring containing zero to three heteroatoms;

wherein each substitutable carbon atom in Ar¹, including the fused ring when present, is optionally and independently substituted by halo, R, OR, SR, OH, NO₂, CN, NH₂, NHR, N(R)₂, NHCOR, NHCONHR, NHCON(R)₂, NRCOR, NHCO₂R, CO₂R, CO₂H, COR, CONHR, CON(R)₂, S(O)₂R, SONH₂, S(O)R, SO₂NHR, or NHS(O)₂R, and wherein each saturated carbon in the fused ring is further optionally and independently substituted by =O, =S, =NNHR, =NNR₂, =N-OR, =NNHCOR, =NNHCO₂R, =NNHSO₂R, or =NR; and

wherein each substitutable nitrogen atom in Ar¹ is optionally substituted by R, COR, S(O)₂R, or CO₂R.

8. The method of claim 7 wherein the disease is selected from inflammatory diseases, autoimmune diseases, destructive bone disorders, proliferative disorders, infectious diseases, neurodegenerative diseases, allergies, reperfusion/ischemia in stroke, heart attacks, angiogenic disorders, organ hypoxia, vascular hyperplasia, cardiac hypertrophy, thrombin-induced platelet aggregation or conditions associated with proinflammatory cytokines.

9. The method according to claim 7, wherein said method is used to treat or prevent an inflammatory disease selected from acute pancreatitis, chronic

pancreatitis, asthma, allergies, or adult respiratory distress syndrome.

10. The method according to claim 7, wherein said method is used to treat or prevent an autoimmune disease selected from glomerulonephritis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Graves' disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, or graft vs. host disease.

11. The method according to claim 7, wherein said method is used to treat or prevent a destructive bone disorders selected from osteoarthritis, osteoporosis or multiple myeloma-related bone disorder.

12. The method according to claim 7, wherein said method is used to treat or prevent a proliferative disease selected from acute myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's sarcoma, or multiple myeloma.

13. The method according to claim 7, wherein said method is used to treat or prevent neurodegenerative disease selected from Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Huntington's disease, cerebral ischemia or neurodegenerative disease

caused by traumatic injury, glutamate neurotoxicity or hypoxia.

14. The method according to claim 7, wherein said method is used to treat or prevent ischemia/reperfusion in stroke or myocardial ischemia, renal ischemia, heart attacks, organ hypoxia or thrombin-induced platelet aggregation.

15. The method according to claim 7, wherein said method is used to treat or prevent a condition associated with T-cell activation or pathologic immune responses.

16. The method according to claim 7, wherein said method is used to treat or prevent an angiogenic disorder selected from solid tumors, ocular neovascularization, or infantile haemangioma.